ACCESS DB # 92211

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PLEASE PRINT CLEARLY

Scientific and Technical Information Center

# SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/20

Art Unit: 1624 Phone Number: 2-0663 Serial Number: 10/519897

Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

**********

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): _____

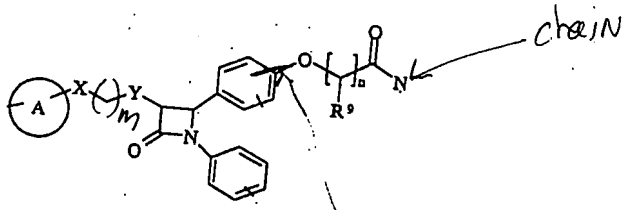
OH-999

Earliest Priority Date: _____

Search Topic:

*Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.*

*For Sequence Searches Only* *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*




A=  carbocyclic

m=1-3 X, Y = C/O/N/S

any position - float

$R^9$ = H / $CH_3$

n=1-4

**********

STAFF USE ONLY

Searcher: _____

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 4/25/07

Searcher Prep & Review Time: _____

Online Time: _____

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

_____ Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

418.45 STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

___ In-house sequence systems

___ Commercial ___ Oligomer ___ Score/Length

___ Interference ___ SPDI ___ Encode/Transl

_____ Other (specify)

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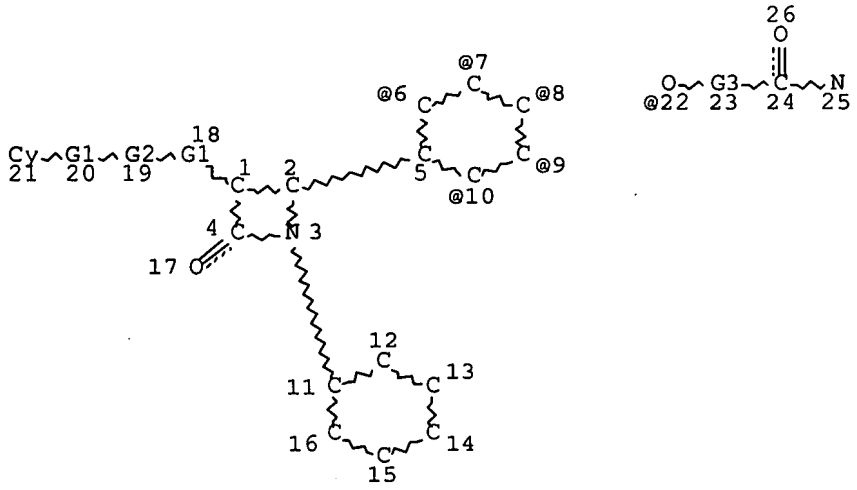

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  26

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L15           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 NOT L14


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L15  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:216794  HCAPLUS  Full-text
DOCUMENT NUMBER:          142:297976
TITLE:                    Preparation of bis- and
```

tris(arylpropyl)(aryl)oxoazetidinylphenyl-substituted compounds as antihypercholesteremic and antihyperlipidemic agents

INVENTOR(S): Martinez, Eduardo J.; Talley, John Jeffrey
PATENT ASSIGNEE(S): Microbia, Inc., USA

SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2005021497 | A2 | 20050310 | WO 2004-US27813 | 20040827 |
| WO 2005021497 | A3 | 20050609 | | |
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| EP 1660446 | A2 | 20060531 | EP 2004-782312 | 20040827 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |

PRIORITY APPLN. INFO.: US 2003-498476P P 20030828
WO 2004-US27813 W 20040827

OTHER SOURCE(S): CASREACT 142:297976; MARPAT 142:297976
ED Entered STN: 11 Mar 2005
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Bis- and tris(arylpropyl)(aryl)oxoazetidinylphenyl-substituted compds. I [m = 0-3; n = 0-1; R1, R2 = H, halo, HO, NC, alkyl, alkoxy, alkylthio, H2N, alkylamino, alkylsulfonyl, arylsulfonyl, acyl, a sugar, a glucuronide, or a sugar carbamate; R3 = H, HO, F, alkoxy; R4 = H, F; R3R4 = O; R5 = H, halo, HO, NC, H2N, alkyl, alkoxy, alkylthio, alkylamino, alkylsulfonyl, arylsulfonyl, acyl; W = XAY or XA(Y)Z; if W = XAY, m + n = 2, otherwise m + n = 3; X, Y, Z = bond, O, S, NH, CH2O, CH2NH, OCH2C(:O)NH, OCH2C(:O)O, C(:O), C(:O)NH, NHC(:O), OC(:O), C(:O)O, NHC(:O)NH, OC(:O)NH, NHC(:O)O] such as II (B = 4-FC6H4) are prepared as antihypercholesteremic and antihyperlipidemic agents for the treatment of hyperlipidemia, arteriosclerosis, or coronary heart disease, for decreasing blood plasma or serum concns. of LDL cholesterol, cholesteryl esters, C-reactive protein, apolipoprotein B, or triglycerides, and for increasing the blood plasma or serum concentration of HDL cholesterol. Nonracemic azetidinone III (R = H) is triflated with N,N-bis(trifluoromethylsulfonyl)aniline in the presence of DMAP to yield III (R = F3CSO2); palladium-catalyzed coupling of III (R = F3CSO2) with 1,4-

benzenediboronic acid yields II (B = 4-FC6H4). No biol. data are provided for I.

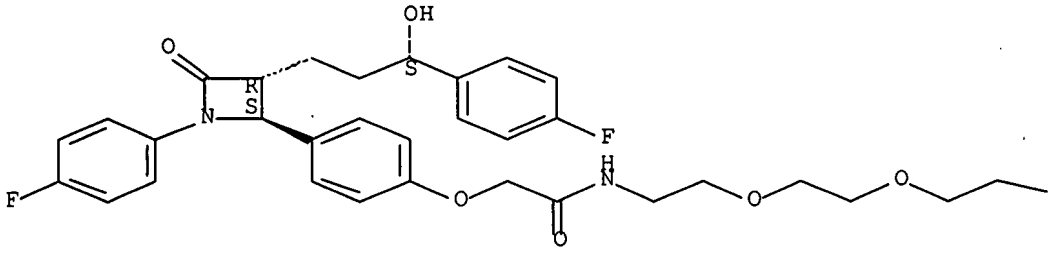
IT **847781-58-2P 847781-69-5P**
(drug candidate; preparation of bis- and tris(arylpropyl)(aryl)oxoazetidinylphenyl-substituted compds. as antihypercholesteremic and antihyperlipidemic agents)

RN 847781-58-2 HCAPLUS

CN Acetamide, N,N'-[1,2-ethanediylbis(oxy-2,1-ethanediyl)]bis[2-[4-[(2S,3R)-1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-oxo-2-azetidinyl]phenoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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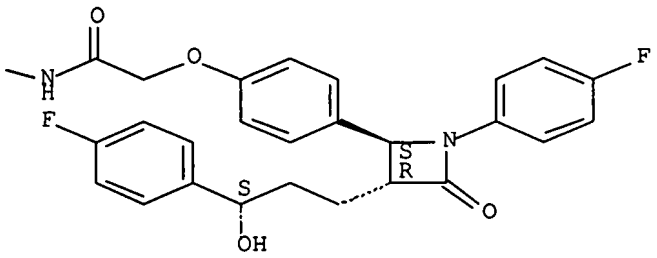

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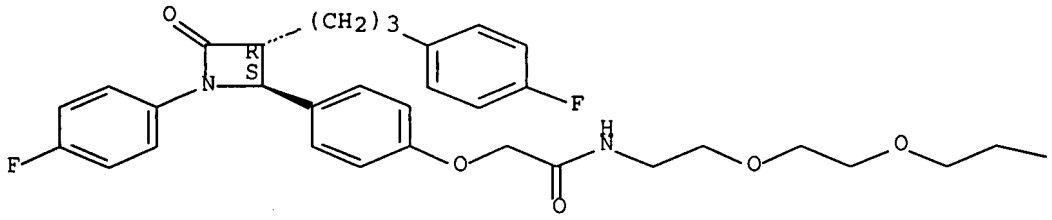
Absolute stereochemistry.

PAGE 1-A



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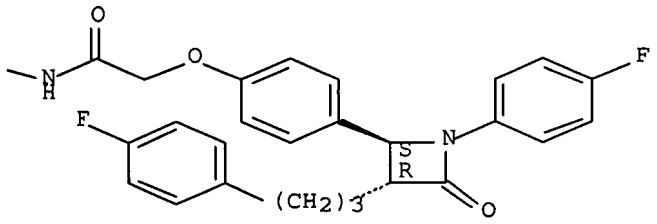

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CC 27-5 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
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847781-54-8P 847781-56-0P **847781-58-2P**
**847781-69-5P**
(drug candidate; preparation of bis- and tris(arylpropyl)(aryl)oxoazetidinylphenyl-substituted compds. as antihypercholesteremic and antihyperlipidemic agents)

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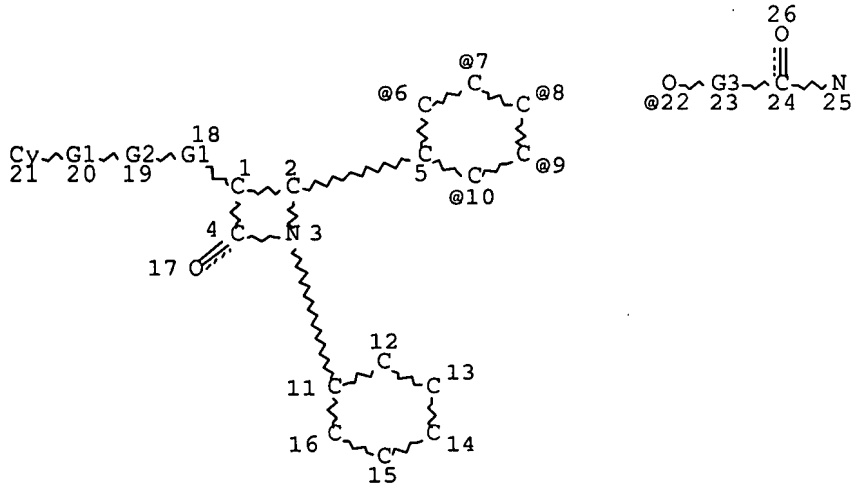

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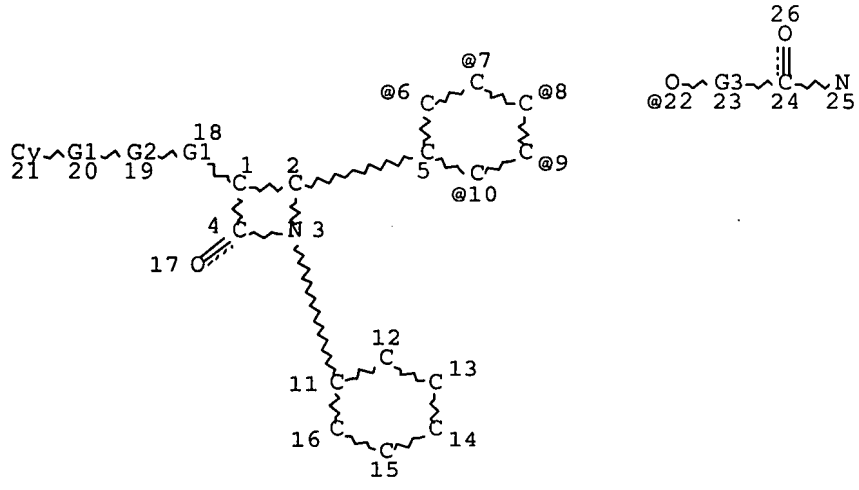

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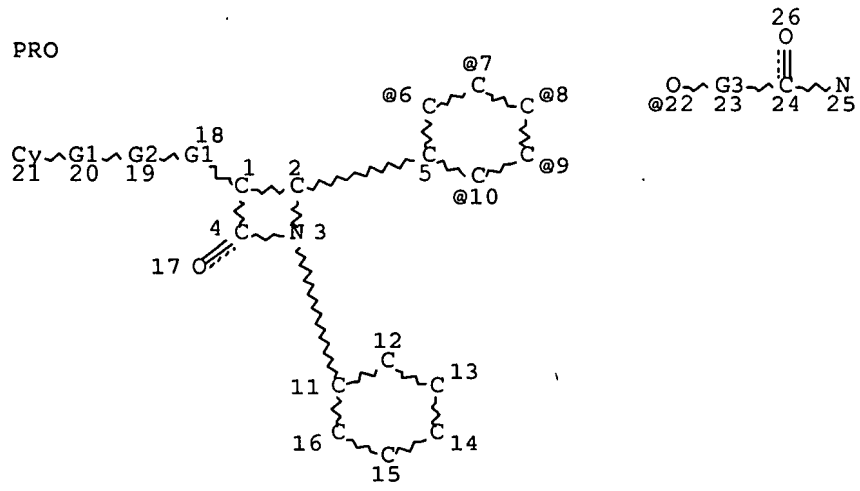


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GRAPH ATTRIBUTES:
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L25 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:297976 CASREACT Full-text
TITLE: Preparation of bis- and tris(arylpropyl)(aryl)oxoazetidinylphenyl-substituted compounds as antihypercholesteremic and antihyperlipidemic agents
INVENTOR(S): Martinez, Eduardo J.; Talley, John Jeffrey
PATENT ASSIGNEE(S): Microbia, Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005021497 | A2 | 20050310 | WO 2004-US27813 | 20040827 |
| WO 2005021497 | A3 | 20050609 | | |
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| EP 1660446 | A2 | 20060531 | EP 2004-782312 | 20040827 |
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PRIORITY APPLN. INFO.: US 2003-498476P 20030828
WO 2004-US27813 20040827
OTHER SOURCE(S): MARPAT 142:297976
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Bis- and tris(arylpropyl)(aryl)oxoazetidinylphenyl-substituted compds. I [m = 0-3; n = 0-1; R1, R2 = H, halo, HO, NC, alkyl, alkoxy, alkylthio, H2N, alkylamino, alkylsulfonyl, arylsulfonyl, acyl, a sugar, a glucuronide, or a sugar carbamate; R3 = H, HO, F, alkoxy; R4 = H, F; R3R4 = O; R5 = H, halo, HO, NC, H2N, alkyl, alkoxy, alkylthio, alkylamino, alkylsulfonyl, arylsulfonyl, acyl; W = XAY or XA(Y)Z; if W = XAY, m + n = 2, otherwise m + n = 3; X, Y, Z = bond, O, S, NH, CH2O, CH2NH, OCH2C(:O)NH, OCH2C(:O)O, C(:O), C(:O)NH, NHC(:O), OC(:O), C(:O)O, NHC(:O)NH, OC(:O)NH, NHC(:O)O] such as II (B = 4-FC6H4) are prepared as antihypercholesteremic and antihyperlipidemic agents for the treatment of hyperlipidemia, arteriosclerosis, or coronary heart disease, for decreasing blood plasma or serum concns. of LDL cholesterol, cholesteryl esters, C-reactive protein, apolipoprotein B, or triglycerides, and for increasing the blood plasma or serum concentration of HDL cholesterol. Nonracemic azetidinone III (R = H) is triflated with N,N-bis(trifluoromethylsulfonyl)aniline in the presence of DMAP to yield III (R = F3CSO2); palladium-catalyzed coupling of III (R = F3CSO2) with 1,4-

benzenediboronic acid yields II (B = 4-FC6H4). No biol. data are provided for I.

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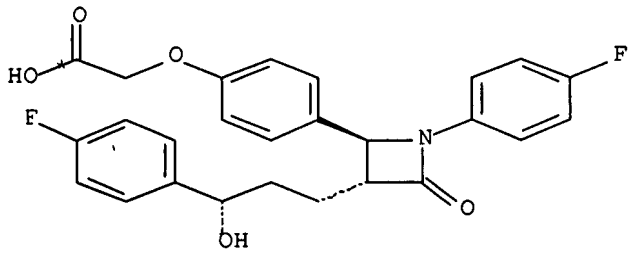

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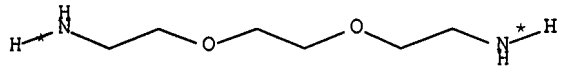

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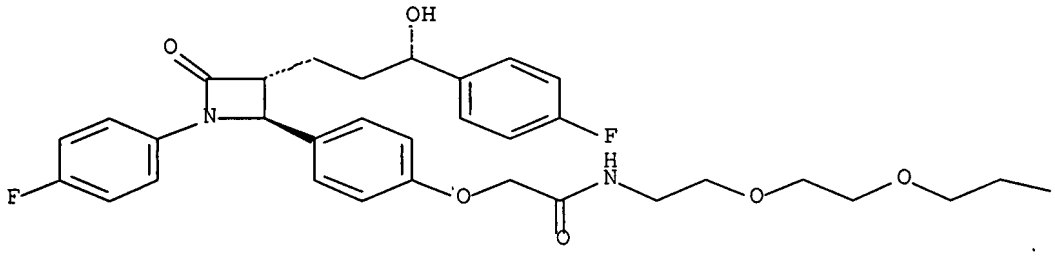

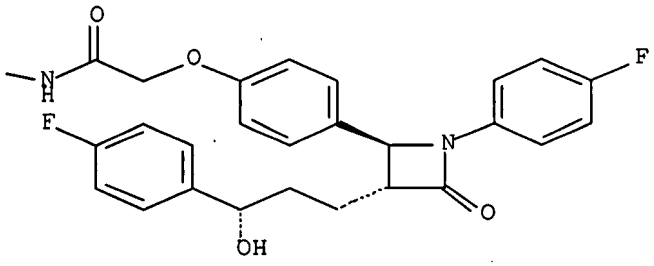

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CON room temperature

PRO AD 847781-58-2

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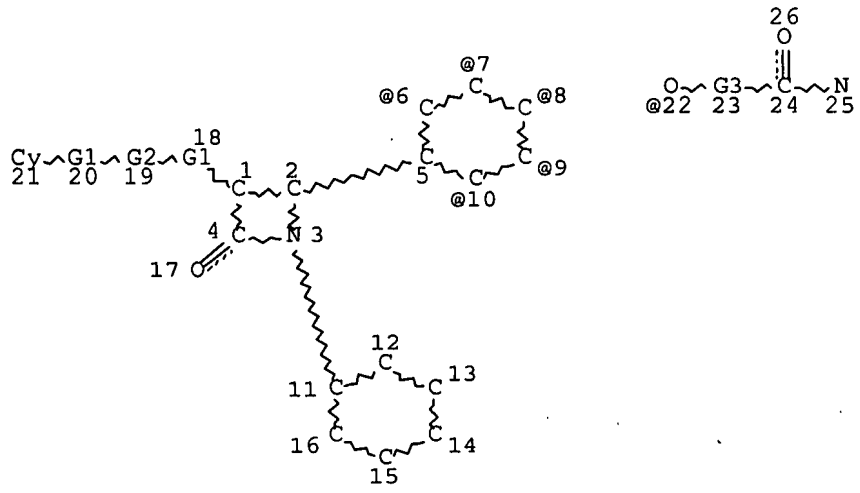

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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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L14  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:1357043  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:101041
TITLE:                    Preparation of novel 2-azetidinone derivatives and
                          their use as cholesterol absorption inhibitors for
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the treatment of hyperlipidaemia

INVENTOR(S): Alenfalk, Susanne; Dahlstroem, Mikael; Hunegnaw, Fana; Karlsson, Staffan; **Lemurell, Malin**; **Lindqvist, Ann-Margret**; Skjaeret, Tore; **Starke, Ingemar**

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137782 | A1 | 20061228 | WO 2006-SE741 | 20060619 |

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PRIORITY APPLN. INFO.: SE 2005-1425 A 20050620

OTHER SOURCE(S): MARPAT 146:101041

ED Entered STN: 29 Dec 2006

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

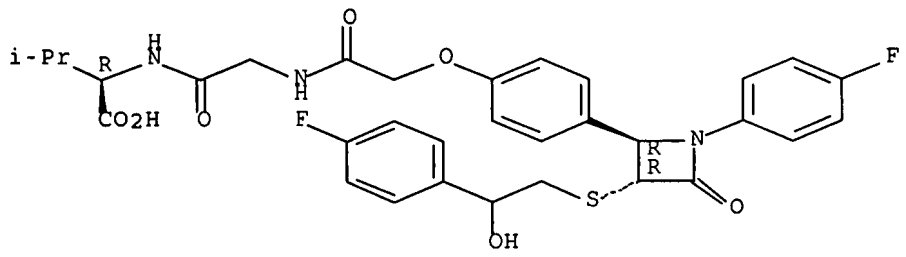
AB Azetidinone compds. I [R1 = H, C1-6-alkyl, C3-6-cycloalkyl, aryl; R2 = H, (un)branched C1-6-alkyl, C3-6-cycloalkyl, aryl; R3 = H, alkyl, halo, C1-6-alkoxy; R4 = H, halo, C1-6-alkoxy; R5 = H, C1-6-alkyl, arylalkyl, aryl(C1-6)-alkyl; R6 = H, C1-6-alkyl, aryl(C1-6)-alkyl; R5R6 = 2-7 carbon atom ring; R2R6 = 3-6 carbon atom ring], pharmaceutically acceptable salts, solvates, solvates of such salts and prodrugs thereof and their use as cholesterol absorption inhibitors for the treatment of hyperlipidemia are described. Processes for their manufacture and pharmaceutical compns. containing them are also described. For example, reacting azetidinyl acetylglycine derivative II with 1-amino-1-cyclopropanecarboxylic acid gave adduct III in 23% yield.

IT **858103-14-7P**
(preparation of 2-azetidinone derivs. as cholesterol absorption inhibitors for treating hyperlipidemia)

RN 858103-14-7 HCAPLUS

CN D-Valine, N-[[4-[(2R,3R)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 26, 63
IT **858103-14-7P 858103-20-5P 858103-29-4P**
**858103-63-6P 858103-85-2P 917601-04-8P**
(preparation of 2-azetidinone derivs. as cholesterol absorption inhibitors for treating hyperlipidemia)
IT 22059-21-8, 1-Amino-1-cyclopropanecarboxylic acid 26782-71-8
27532-96-3, tert-Butyl glycinate hydrochloride 39741-62-3
58717-02-5 115692-31-4 179559-35-4, O-(tert-Butyl)-D-serine tert-butyl ester hydrochloride 212140-39-1 **858103-90-9**
858104-50-4 **858104-55-9** 858104-61-7 858104-97-9
(preparation of 2-azetidinone derivs. as cholesterol absorption inhibitors for treating hyperlipidemia)
IT **858104-35-5P** 858104-40-2P, β,β-Dimethyl-D-phenylalanine trifluoroacetate **858104-94-6P**
**917601-01-5P 917601-02-6P 917601-05-9P**
**917601-06-0P**
(preparation of 2-azetidinone derivs. as cholesterol absorption inhibitors for treating hyperlipidemia)
IT **858104-62-8P 858104-63-9P 858104-64-0P**
**858104-65-1P 917600-99-8P 917601-00-4P**
(preparation of 2-azetidinone derivs. as cholesterol absorption inhibitors for treating hyperlipidemia)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1357032 HCAPLUS Full-text
DOCUMENT NUMBER: 146:100481
TITLE: Preparation of novel 2-azetidinone derivatives as cholesterol absorption inhibitors for the treatment of hyperlipidaemic conditions
INVENTOR(S): Dahlstroem, Mikael; Hunegnaw, Fana; **Lemurell, Malin**; Nordberg, Peter; Skjaeret, Tore; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 108pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137795 | A1 | 20061228 | WO 2006-SE764 | 20060621 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

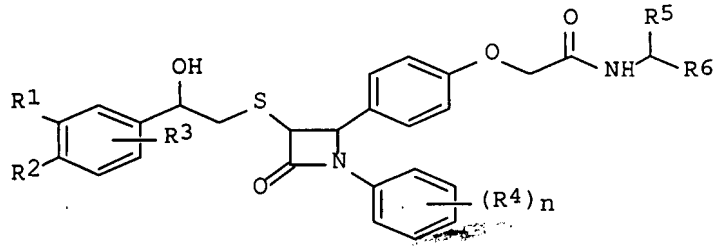
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1466 A 20050622

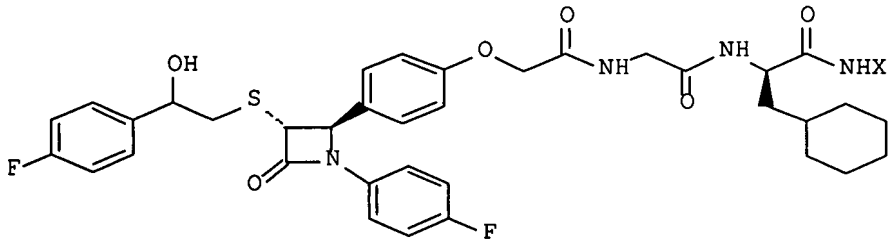
OTHER SOURCE(S): MARPAT 146:100481

ED Entered STN: 29 Dec 2006

GI



I



II

AB Novel 2-azetidinone derivs. of formula I [R1, R2 = H, alkyl, cycloalkyl, aryl; R3 = halo, OH, alkyl, alkoxy, etc.; R4 = halo, nitro, CN, OH, amino, CO2H, CHO, etc.; R5 = H, halo, nitro, CN, OH, amino, SH, alkyl, etc.; R6 = H, alkyl, cycloalkyl, aryl; n = 1-5] are prepared The compds. are cholesterol absorption inhibitors and are useful in the treatment of hyperlipidemic conditions, including atherosclerosis, Alzheimers' disease and cholesterol associated tumors. The application also relates to pharmaceutical formulations comprising such compds. and to processes for their preparation Thus, II (X = CH2CH2N+Me3 acetate) was prepared, and had Caco value of 0.61x10-6 cm/s in absorption assay.

IT **917753-18-5P**

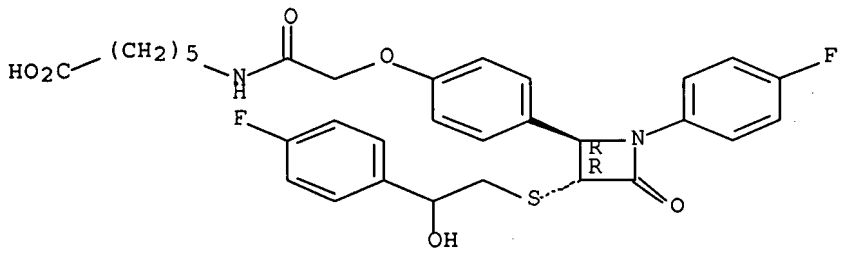
(preparation of azetidinone derivs. as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

RN 917753-18-5 HCAPLUS

CN Hexanoic acid, 6-[[2-[4-[(2R,3R)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxo-2-

azetidinyl]phenoxy]acetyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.



CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63

IT **917753-18-5P 917753-20-9P**
(preparation of azetidinone derivs. as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT **917752-98-8P 917752-99-9P 917753-00-5P**
**917753-01-6P 917753-02-7P 917753-03-8P**
**917753-04-9P 917753-05-0P 917753-06-1P**
**917753-07-2P 917753-08-3P 917753-09-4P**
**917753-10-7P 917753-11-8P 917753-12-9P**
**917753-13-0P 917753-15-2P 917753-16-3P**
**917753-17-4P 917753-19-6P 917753-21-0P**
**917753-22-1P 917753-23-2P 917753-24-3P**
**917753-25-4P**
(preparation of azetidinone derivs. as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT 56-12-2, 4-Aminobutyric acid, reactions 60-32-2, 6-Aminohexanoic acid 107-95-9, 3-Aminopropionic acid 488-43-7, D-Glucamine 498-94-2, 4-Piperidinecarboxylic acid 536-38-9, 2-Bromo-1-(4-chlorophenyl)ethanone 640-68-6, D-Valine 660-88-8, 5-Aminovaleric acid 3399-67-5 4530-20-5, N-(tert-Butoxycarbonyl)glycine 21691-52-1 27532-96-3 31202-69-4 34722-37-7, [(4-Methoxybenzyl)thio]acetic acid 58620-93-2 58717-02-5 62024-63-9 68206-45-1, 3-Nitro-2-pyridinesulfenyl chloride 89711-08-0, tert-Butyl (2-oxoethyl)carbamate 91900-05-9 99395-88-7, (S)-(+)-4-Phenyl-2-oxazolidinone 104944-18-5 106719-44-2 112245-09-7 129042-71-3 166023-31-0 204191-43-5, 3-Amino-4,4-dimethylpentanoic acid 205178-80-9 **858103-29-4** **858104-00-4** **858104-35-5** 858104-50-4 917577-63-0 **917601-01-5** 917753-34-5 917753-35-6
(preparation of azetidinone derivs. as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT 857506-73-1P **858103-94-3P** 858104-45-7P 858104-46-8P 858104-47-9P 858104-48-0P **858104-55-9P** 917753-26-5P 917753-27-6P 917753-28-7P 917753-29-8P **917753-30-1P** 917753-31-2P 917753-32-3P **917753-33-4P** **917753-36-7P**
(preparation of azetidinone derivs. as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

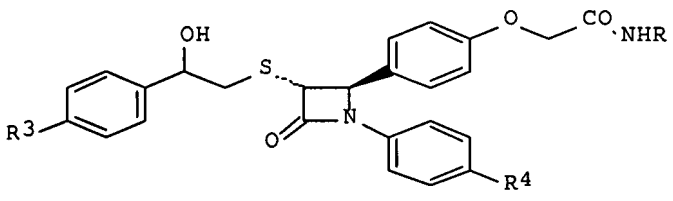
L14 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1356820 HCAPLUS Full-text
DOCUMENT NUMBER: 146:100480
TITLE: New 2-azetidinone derivatives for the treatment of hyperlipidemic diseases
INVENTOR(S): Dahlstroem, Mikael; Hunegnaw, Fana; Karlsson, Staffan; Nordberg, Peter; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137794 | A1 | 20061228 | WO 2006-SE763 | 20060621 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1467 A 20050622

OTHER SOURCE(S): MARPAT 146:100480
ED Entered STN: 29 Dec 2006
GI

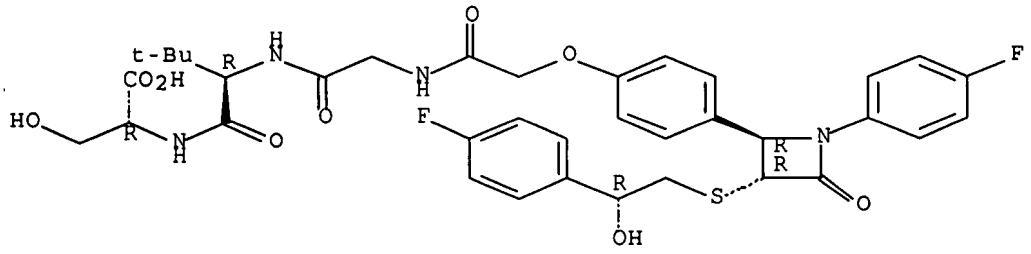



I

AB 2-Azetidinone derivs., such as I [NHR = peptide residue; R3, R4 = H, halogen, alkyl, alkoxy], were prepared for use in pharmaceutical compns. which inhibit absorption of cholesterol and are useful in the treatment of hyperlipidemic conditions, atherosclerosis and Alzheimer's disease. Thus, I [NHR = Gly-(R)-NHCH(Ph)CO-Gly-OH, R3 = R4 = F] was prepared via an amidation reaction of I [NHR = Gly-(R)-NHCH(Ph)CO2H, R3 = R4 = F] with glycine tert-Bu ester using N-methylmorpholine and TBTU in CH2Cl2 followed by treatment of the reaction mixture with HCO2H. The prepared azetidinones were tested for their effect on cholesterol absorption in a Caco-2 cell model.

IT **917783-65-4P**
(claimed compound; preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
RN 917783-65-4 HCAPLUS
CN D-Serine, N-[2-[4-[(2R,3R)-1-(4-fluorophenyl)-3-[[(2R)-2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl-3-methyl-D-valyl- (CA INDEX NAME)

Absolute stereochemistry.



CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63
IT **917783-65-4P 917783-67-6P 917783-69-8P**
**917783-71-2P 917783-73-4P 917783-75-6P**
(claimed compound; preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
IT **917782-89-9P 917782-92-4P 917782-95-7P**
**917782-97-9P 917782-99-1P 917783-03-0P**
**917783-08-5P 917783-13-2P 917783-18-7P**
**917783-20-1P 917783-22-3P 917783-25-6P**
**917783-28-9P 917783-30-3P 917783-32-5P**
**917783-35-8P 917783-40-5P 917783-42-7P**
**917783-45-0P**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
IT 56-40-6, Glycine, reactions 72-18-4, L-Valine, reactions 95-77-2, 3,4-Dichlorophenol 106-48-9, 4-Chlorophenol 338-69-2, D-Alanine 627-01-0, N-Ethylglycine 640-68-6, D-Valine 673-06-3, D-Phenylalanine 875-74-1 2058-58-4, D-Asparagine 2776-60-5, Glycylglycine methyl ester hydrochloride 6456-74-2 17136-36-6, N-Benzylglycine 22818-40-2, D-4-Hydroxyphenylglycine 26782-71-8, D-tert-Leucine 27532-96-3, tert-Butyl glycinate hydrochloride 37535-58-3 58717-02-5 158000-11-4 179559-35-4 212140-39-1
**858102-84-8 858103-29-4 858103-63-6**
858104-50-4 **858104-57-1 917601-01-5** 917753-34-5
917783-37-0 **917783-50-7 917783-56-3** 917783-63-2
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
IT **858103-14-7P 858103-89-6P 858104-06-0P**
**917601-02-6P 917783-06-3P 917783-11-0P**
**917783-16-5P 917783-48-3P 917783-54-1P**
917783-60-9P
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

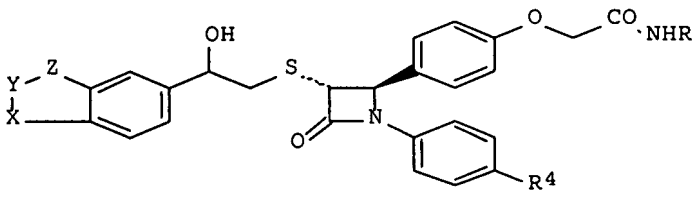
L14 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1356585 HCAPLUS Full-text
DOCUMENT NUMBER: 146:100479
TITLE: New 2-azetidinone derivatives useful in the treatment of hyperlipidemic conditions
INVENTOR(S): Dahlstroem, Mikael; Karlsson, Staffan; **Lemurell, Malin**; Nordberg, Peter; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137792 | A1 | 20061228 | WO 2006-SE761 | 20060621 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1469 A 20050622

OTHER SOURCE(S): MARPAT 146:100479
ED Entered STN: 29 Dec 2006
GI




I

AB 2-Azetidinone derivs., such as I [NHR = peptide residue; R4 = H, halogen, alkyl, alkoxy; X = CH2, O; Y = (CH2)n, n = 1, 2, 3; Z = CH2, O], were prepared for use in pharmaceutical compns. which inhibit absorption of cholesterol and are useful in the treatment of hyperlipidemic conditions, atherosclerosis and Alzheimer's disease. Thus, I [NHR = Gly-X1-Gly-OH, X1 = 3-cyclohexyl-D-alanyl,

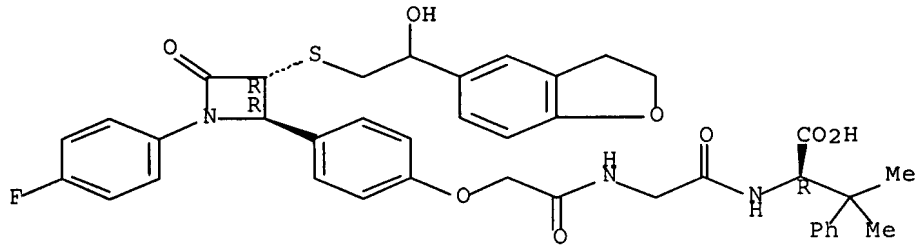
R4 = F, X-Y-Z = (CH2)3] was prepared via a multistep synthesis starting from 2-bromo-1-(2,3-dihydro-1H-inden-5-yl)ethanone, tert-Bu (4-formylphenoxy)acetate, F-4-C6H4NH2, Me3CCONHCH2CO2Me.HCl and Me 3-cyclohexyl-D-alaninate hydrochloride.

IT **917602-84-7**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

RN 917602-84-7 HCAPLUS

CN D-Phenylalanine, N-[2-[4-[(2R,3R)-3-[[2-(2,3-dihydro-5-benzofuranyl)-2-hydroxyethyl]thio]-1-(4-fluorophenyl)-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl-β,β-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.



CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63

IT 95-77-2, 3,4-Dichlorophenol 371-40-4, 4-Fluoroaniline 4530-20-5, N-(tert-Butoxycarbonyl)glycine 6456-74-2, tert-Butyl glycinate 27532-96-3, tert-Butyl glycinate hydrochloride 34722-37-7, [(4-Methoxybenzyl)thio]acetic acid 39696-16-7, 2-Bromo-1-(2,3-dihydro-1H-inden-5-yl)ethanone 68206-45-1, 3-Nitro-2-pyridinesulfenyl chloride 99395-88-7, (S)-(+)-4-Phenyl-2-oxazolidinone 144644-00-8 276884-77-6 **917602-84-7**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT 858104-45-7P 858104-46-8P 858104-47-9P 858104-48-0P 917577-60-7P 917577-63-0P 917577-70-9P 917577-73-2P **917602-85-8P** 917602-87-0P
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT **917602-83-6P 917602-86-9P**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1356557 HCAPLUS Full-text
DOCUMENT NUMBER: 146:100478
TITLE: Novel 2-azetidinone derivatives as cholesterol absorption inhibitors for the treatment of hyperlipidemic conditions
INVENTOR(S): Alenfalk, Susanne; Dahlstroem, Mikael; Hunegnaw, Fana; Karlsson, Staffan; **Lemurell, Malin**; **Starke, Ingemar**

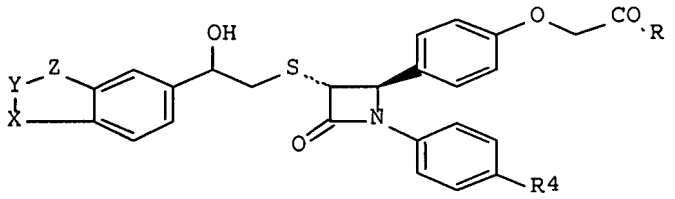
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 107pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137796 | A1 | 20061228 | WO 2006-SE765 | 20060621 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1465 A 20050622

OTHER SOURCE(S): MARPAT 146:100478
ED Entered STN: 29 Dec 2006
GI

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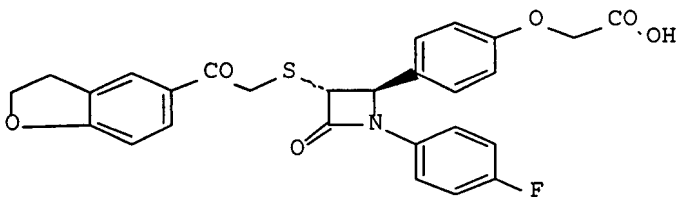



II

AB 2-Azetidinone derivs., such as I [R = peptide residue; R4 = H, halogen, alkyl, alkoxy; X = CH2, O; Y = (CH2)n, n = 1, 2, 3; Z = CH2, O], were prepared for use in pharmaceutical compns. which inhibit absorption of cholesterol and are useful in the treatment of hyperlipidemic conditions, atherosclerosis and Alzheimer's disease. Thus, I [R = Gly-X1-OH, X1 = 3-cyclohexyl-D-alanyl, R4 = F, X-Y-Z = O(CH2)2] was prepared via and amidation reaction of acid II with glycyl-3-cyclohexyl-D-alanine using N-methylmorpholine and TBTU in DMF followed by reduction of the intermediate ketone using NaBH4 in MeOH. The

prepared azetidinones were tested for inhibition of cholesterol absorption using a Caco-2 cell model.

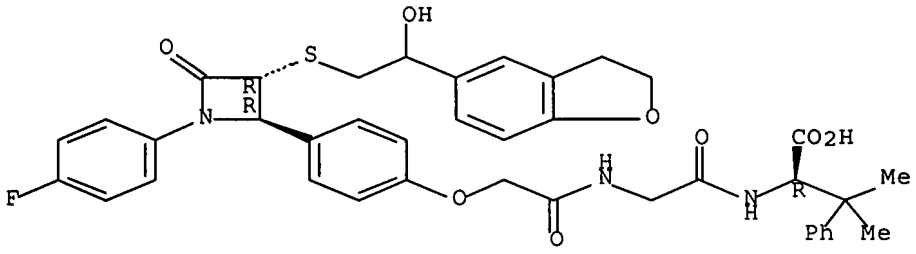
IT **917602-84-7P**

(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

RN 917602-84-7 HCAPLUS

CN D-Phenylalanine, N-[2-[4-[(2R,3R)-3-[[2-(2,3-dihydro-5-benzofuranyl)-2-hydroxyethyl]thio]-1-(4-fluorophenyl)-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl-β,β-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.




CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63

IT **917602-84-7P 917814-85-8P 917814-87-0P**
**917814-88-1P 917814-90-5P 917814-91-6P**
**917814-94-9P 917814-97-2P 917814-99-4P**
**917815-01-1P 917815-03-3P 917815-05-5P**

(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT 95-77-2, 3,4-Dichlorophenol 106-48-9, 4-Chlorophenol 371-40-4, 4-Fluoroaniline 4530-20-5, N-(tert-Butoxycarbonyl)glycine 5680-79-5, Methyl glycinate hydrochloride 5896-66-2, 2-Bromo-1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethanone 26782-71-8 27532-96-3, tert-Butyl glycinate hydrochloride 34722-37-7, [(4-Methoxybenzyl)thio]acetic acid 39696-16-7 53940-82-2 58717-02-5 64089-34-5 68206-45-1, 3-Nitro-2-pyridinesulfenyl chloride 79416-87-8 99395-88-7, (S)-(+)-4-Phenyl-2-oxazolidinone 146727-61-9 189035-22-1, 6-Bromo-2,3-dihydrobenzofuran 201007-86-5 276884-77-6 857506-73-1 858104-40-2 917783-63-2
**917815-02-2**

(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT 374706-07-7P 858104-45-7P 858104-46-8P 858104-47-9P
858104-48-0P 917577-63-0P 917602-87-0P 917814-86-9P
**917814-89-2P** 917814-92-7P 917814-93-8P
**917814-95-0P 917814-96-1P 917814-98-3P**
**917815-00-0P 917815-04-4P 917815-06-6P**
**917815-07-7P** 917815-08-8P **917815-09-9P**
917815-10-2P 917815-11-3P **917815-12-4P** 917815-13-5P
**917815-14-6P 917815-15-7P 917815-16-8P**
917815-17-9P 917815-18-0P

(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

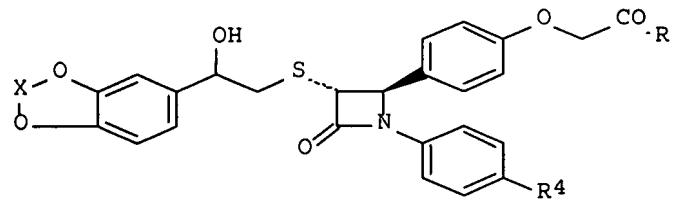
L14 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1354329 HCAPLUS Full-text
DOCUMENT NUMBER: 146:100477
TITLE: Novel 2-azetidinone derivatives as cholesterol absorption inhibitors for the treatment of hyperlipidemic conditions
INVENTOR(S): Alenfalk, Susanne; Dahlstroem, Mikael; Hunegnaw, Fana; Karlsson, Staffan; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 105pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137797 | A1 | 20061228 | WO 2006-SE766 | 20060621 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1464 A 20050622

OTHER SOURCE(S): MARPAT 146:100477
ED Entered STN: 28 Dec 2006
GI

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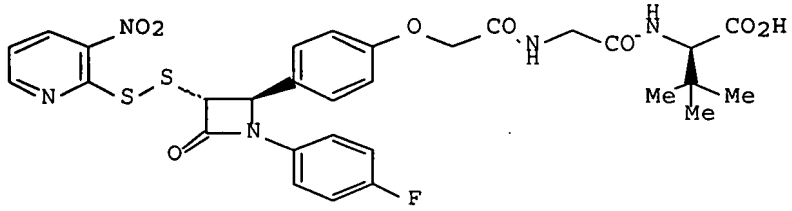



II

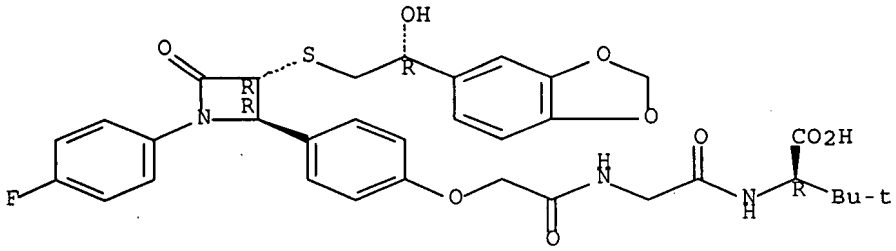
AB 2-Azetidinone derivs., such as I [R = peptide residue; R4 = H, halogen, alkyl, alkoxy; X = (CH2)n, n = 1, 2, 3], were prepared for use in pharmaceutical compns. which inhibit absorption of cholesterol and are useful in the treatment of hyperlipidemic conditions, atherosclerosis and Alzheimer's disease. Thus, I [R = Gly-3-methyl-D-Val-OH, R4 = F, X = (CH2)2] was prepared by treating disulfide II with PPh3 in Me2CO and H2O followed by addition to the reaction mixture of 2-bromo-1-(2,3-dihydro-1,4-benzodioxin-6-yl)ethanone and Et3N in CH2Cl2 and then addn of NaBH4 to the reaction mixture The prepared azetidinones were tested for inhibition of cholesterol absorption using a Caco-3 cell model.

IT **917887-15-1P**
(claimed compound; preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

RN 917887-15-1 HCAPLUS

CN D-Valine, N-[2-[4-[(2R,3R)-3-[[(2R)-2-(1,3-benzodioxol-5-yl)-2-hydroxyethyl]thio]-1-(4-fluorophenyl)-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl-3-methyl- (CA INDEX NAME)

Absolute stereochemistry.



CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63

IT **917887-15-1P 917887-16-2P**
(claimed compound; preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT 857506-72-0P 857506-73-1P 858104-27-5P 858104-45-7P
858104-46-8P 858104-47-9P 917577-58-3P 917577-63-0P
917886-78-3P 917886-80-7P 917886-82-9P **917886-84-1P**
**917886-89-6P** 917886-91-0P 917886-95-4P 917886-96-5P
**917886-97-6P** 917886-99-8P 917887-01-5P 917887-03-7P
917887-04-8P 917887-05-9P 917887-06-0P 917887-07-1P
917887-08-2P 917887-09-3P 917887-10-6P 917887-11-7P
917887-12-8P 917887-13-9P 917887-14-0P
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

IT **917886-77-2P 917886-79-4P 917886-81-8P**
**917886-83-0P 917886-85-2P 917886-86-3P**
**917886-88-5P 917886-90-9P 917886-92-1P**
**917886-93-2P 917886-94-3P**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

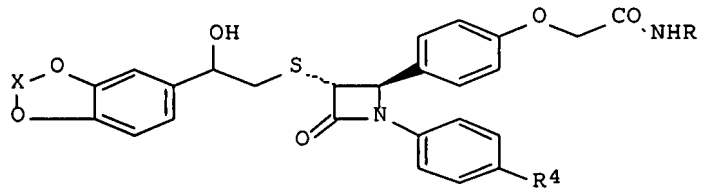
L14 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1354233 HCAPLUS Full-text
DOCUMENT NUMBER: 146:100476
TITLE: New 2-azetidinone derivatives as cholesterol absorption inhibitors for the treatment of hyperlipidemic conditions
INVENTOR(S): Dahlstroem, Mikael; Karlsson, Staffan; Nordberg, Peter; Skjaeret, Tore; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006137793 | A1 | 20061228 | WO 2006-SE762 | 20060621 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1468 A 20050622

OTHER SOURCE(S): MARPAT 146:100476
ED Entered STN: 28 Dec 2006
GI



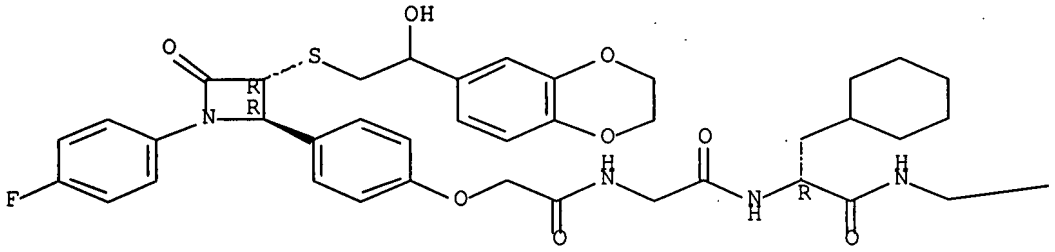

I

AB 2-Azetidinone derivs., such as I [NHR = peptide residue; R4 = H, halogen, alkyl, alkoxy; X = (CH2)n, n = 1, 2], were prepared for use in pharmaceutical compns. which inhibit absorption of cholesterol and are useful in the treatment of hyperlipidemic conditions, atherosclerosis and Alzheimer's disease. Thus, I [NHR = Gly-X1-Gly-OH, X1 = 3-cycloxhexyl-D-alanyl, R4 = F, X = (CH2)2] was prepared via a multistep synthesis starting from 2-bromo-1-(2,3-dihydro-1,4-benzodioxin-6- yl)ethanone, tert-Bu (4-formylphenoxy)acetate, F-4-C6H4NH2, Me3CCONHCH2CO2Me.HCl and Me 3-cyclohexyl-D-alaninate hydrochloride.

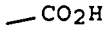
IT **917577-56-1P**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
RN 917577-56-1 HCAPLUS
CN Glycine, N-[2-[4-[(2R,3R)-3-[[2-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-hydroxyethyl]thio]-1-(4-fluorophenyl)-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl-3-cyclohexyl-D-alanyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63
IT **917577-56-1P**
(preparation of 2-azetidinone derivs. for therapeutic use as cholesterol absorption inhibitors for treatment of hyperlipidemic conditions)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

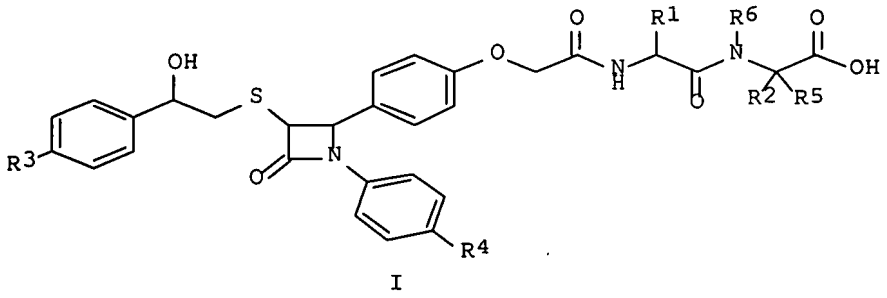
L14 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:588892 HCAPLUS Full-text
DOCUMENT NUMBER: 143:133694
TITLE: Preparation of diphenylazetidinone amino acid derivatives having cholesterol absorption inhibitory activity
INVENTOR(S): Alenfalk, Susanne; Dahlstroem, Mikael; Hunegnaw, Fana; Karlsson, Staffan; **Lemurell, Malin**; **Lindqvist, Ann-Margret**; Skjaeret, Tore; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005061452 | A1 | 20050707 | WO 2004-SE1960 | 20041221 |
| WO 2005061452 | A8 | 20060406 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004303742 | A1 | 20050707 | AU 2004-303742 | 20041221 |
| CA 2550215 | A1 | 20050707 | CA 2004-2550215 | 20041221 |
| EP 1699759 | A1 | 20060913 | EP 2004-809133 | 20041221 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU | | | | |
| NO 2006002591 | A | 20060920 | NO 2006-2591 | 20060606 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | GB 2003-29780 | A | 20031223 |
| | SE 2004-1907 | A | 20040721 |
| | SE 2004-2785 | A | 20041115 |
| | WO 2004-SE1960 | W | 20041221 |

OTHER SOURCE(S): MARPAT 143:133694
ED Entered STN: 08 Jul 2005
GI




I

AB The invention relates to diphenylazetidinones I [R1, R2, R5 are independently H, (un)substituted alkyl, cycloalkyl or aryl; R3 is H, alkyl, halo, alkoxy or

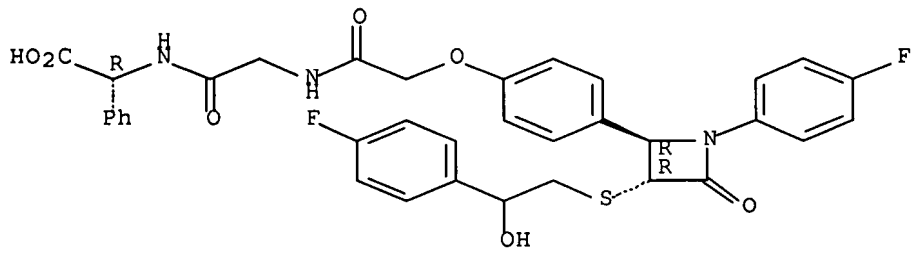
alkylthio; R4 is H, alkyl, halo or alkoxy; R6 is H, alkyl or arylalkyl; or R2 may form a ring with R5 or R6], or their pharmaceutically-acceptable salts, solvates, and prodrugs, and their use as cholesterol absorption inhibitors for the treatment of hyperlipidemia. Thus, 2-azetidinone I [R3, R4 = F; NHCHR1CONR6CR2R5CO2H = Gly-L-Ser-OH (R-configuration at 3- and 4-positions of the azetidine ring)], prepared by peptide coupling and LiAlH4 reduction of the benzoyl oxo group, showed 87% inhibition of 14C-cholesterol absorption.

IT **858102-84-8P**
(preparation of diphenylazetidinone amino acid derivs. having cholesterol absorption inhibitory activity)

RN 858102-84-8 HCAPLUS

CN Glycine, N-[[4-[(2R,3R)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxo-2-azetidinyl]phenoxy]acetyl]glycyl-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D205-08
ICS A61K031-397; A61P003-06; A61P009-10; A61P025-28

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27

IT **858102-84-8P 858102-85-9P 858102-86-0P**
**858102-87-1P 858102-88-2P 858102-89-3P**
**858102-90-6P 858102-91-7P 858102-92-8P**
**858102-93-9P 858102-94-0P 858102-96-2P**
**858102-98-4P 858103-00-1P 858103-02-3P**
**858103-04-5P 858103-06-7P 858103-08-9P**
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858103-84-1P 858103-85-2P 858103-86-3P
858103-87-4P 858103-88-5P 858103-89-6P
858108-28-8P
(preparation of diphenylazetidinone amino acid derivs. having cholesterol absorption inhibitory activity)

IT 857506-72-0P 857506-73-1P 857506-74-2P 857506-75-3P
858103-90-9P 858103-91-0P 858103-92-1P
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(preparation of diphenylazetidinone amino acid derivs. having cholesterol absorption inhibitory activity)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:588890 HCAPLUS Full-text
DOCUMENT NUMBER: 143:115797
TITLE: Preparation of diphenylazetidinone amino acid derivatives having cholesterol absorption inhibitory activity
INVENTOR(S): Alenfalk, Susanne; Dahlstroem, Mikael; Hunegnaw, Fana; Karlsson, Staffan; **Lemurell, Malin**; **Lindqvist, Ann-Margret**; Skjaeret, Tore; **Starke, Ingemar**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005061451 | A1 | 20050707 | WO 2004-SE1959 | 20041221 |
| WO 2005061451 | A8 | 20060406 | | |
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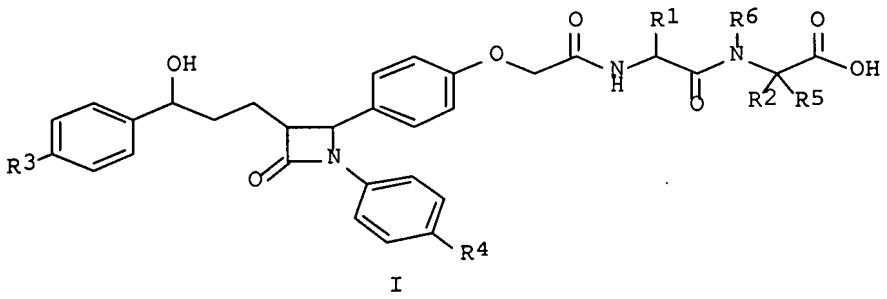
| AU 2004303741 | A1 | 20050707 | AU 2004-303741 | 20041221 |
| CA 2548410 | A1 | 20050707 | CA 2004-2548410 | 20041221 |
| EP 1699758 | A1 | 20060913 | EP 2004-809132 | 20041221 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU | | | | |
| CN 1898203 | A | 20070117 | CN 2004-80038434 | 20041221 |
| NO 2006002583 | A | 20060920 | NO 2006-2583 | 20060606 |
| PRIORITY APPLN. INFO.: | | | GB 2003-29778 A | 20031223 |
| | | | WO 2004-SE1959 W | 20041221 |

OTHER SOURCE(S): MARPAT 143:115797
ED Entered STN: 08 Jul 2005
GI




I

AB The invention relates to diphenylazetidinones I [R1, R2, R5 are independently H, (un)substituted alkyl, cycloalkyl or aryl; R3 is H, alkyl, halo, alkoxy or alkylthio; R4 is H, alkyl, halo or alkoxy; R6 is H, alkyl or arylalkyl; or R2 may form a ring with R5 or R6], or their pharmaceutically-acceptable salts,

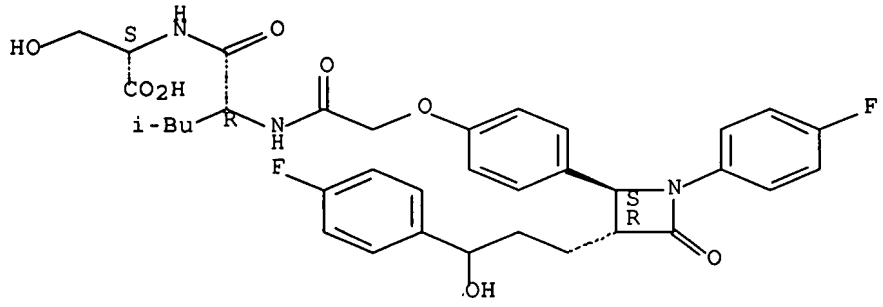
solvates, and prodrugs, and their use as cholesterol absorption inhibitors for the treatment of hyperlipidemia. Thus, 2-azetidinone I [R3, R4 = F; NHCHR1CONR6CR2R5CO2H = D-Leu-L-Ser-OH (R- and S-configuration at 3- and 4-positions of the ring, resp.)] was prepared by coupling of 1-(4-fluorophenyl)-3(R)-[2-(4-fluorobenzoyl)ethyl]-4(S)-[4-[N-[(R)-1- carboxy-3-methylbutyl]carbamoylmethoxy]phenyl]azetidin-2-one with tert-Bu O-tert-butyl-L-serinate hydrochloride, followed by LiAlH4 reduction of the benzoyl oxo group.

IT **857506-52-6P**
(preparation of diphenylazetidinone amino acid derivs. having cholesterol absorption inhibitory activity)

RN 857506-52-6 HCAPLUS

CN L-Serine, N-[[4-[(2S,3R)-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-oxo-2-azetidinyl]phenoxy]acetyl]-D-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D205-08
ICS A61K031-397; A61P003-06; A61P009-10; A61P025-28

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27

IT **857506-52-6P 857506-53-7P 857506-54-8P**
**857506-55-9P 857506-59-3P 857506-60-6P**
**857506-61-7P 857506-62-8P**
(preparation of diphenylazetidinone amino acid derivs. having cholesterol absorption inhibitory activity)

IT 847781-66-2P **857506-56-0P 857506-57-1P**
**857506-58-2P** 857506-63-9P **857506-64-0P**
**857506-65-1P 857506-66-2P 857506-67-3P**
857506-68-4P **857506-69-5P 857506-70-8P**
857506-72-0P 857506-73-1P 857506-74-2P 857506-75-3P
857506-76-4P **857506-77-5P 857506-78-6P**
**857506-79-7P 857506-80-0P**
(preparation of diphenylazetidinone amino acid derivs. having cholesterol absorption inhibitory activity)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41434 HCAPLUS Full-text
DOCUMENT NUMBER: 140:111687
TITLE: Preparation of diphenylazetidinone peptide derivatives for treating disorders of lipid

metabolism

INVENTOR(S): **Starke, Ingemar; Dahlstrom, Mikael Ulf Johan; Lindqvist, Ann-Margret; Nordberg, Mats Peter; Skjaret, Tore; Lemurell, Malin Anita**

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2004005247 | A1 | 20040115 | WO 2003-GB2811 | | 20030701 |
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| CA 2491789 | A1 | 20040115 | CA 2003-2491789 | | 20030701 |
| AU 2003242850 | A1 | 20040123 | AU 2003-242850 | | 20030701 |
| BR 2003012280 | A | 20050412 | BR 2003-12280 | | 20030701 |
| EP 1521742 | A1 | 20050413 | EP 2003-762763 | | 20030701 |
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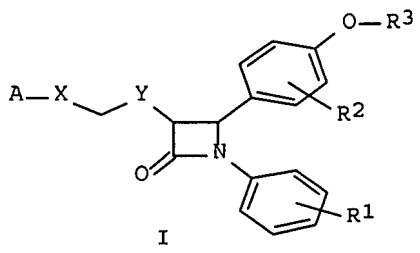
| CN 1665783 | A | 20050907 | CN 2003-815894 | | 20030701 |
| JP 2006501184 | T | 20060112 | JP 2004-518920 | | 20030701 |
| ZA 2004010340 | A | 20051020 | ZA 2004-10340 | | 20041222 |
| US 2005239766 | A1 | 20051027 | US 2004-519897 | | 20041231 |
| NO 2005000016 | A | 20050301 | NO 2005-16 | | 20050103 |
| PRIORITY APPLN. INFO.: | | | GB 2002-15579 | A | 20020705 |
| | | | WO 2003-GB2811 | W | 20030701 |

OTHER SOURCE(S): MARPAT 140:111687

ED Entered STN: 18 Jan 2004

GI



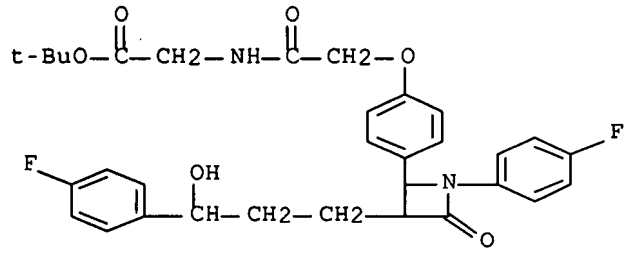

I

AB Azetidinone derivs. I [A is (un)substituted Ph or thienyl; X, Y are (un)substituted methylene, O, NH, alkylimino, S, SO, or SO2; R1, R2 are H, halo, nitro, cyano, etc.; R3 is (CHR4)1-2CONR5CR6R7(CHR8)0-2R9, where R4, R6, R7, R8 are H, (un)substituted alkyl, carbocyclyl, or heterocyclyl or R6R7 is alkylene; R5 is H or alkyl; R9 is H, halo, nitro, amino, carbamoyl, sulfamoyl, hydroxyaminocarbonyl, alk(en)(yn)yl, alkoxy, alkoxycarbonyl, alkylamino, etc.] or their pharmaceutically-acceptable salts or prodrugs were prepared for use as cholesterol absorption inhibitors for the treatment of hyperlipidemia. Thus, 1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-carboxymethoxyphenyl)azetidin-2-one and tert-Bu N-[(2R)-2-amino-2-phenylethanoyl]glycinate were prepared and reacted to form the carboxamide.

IT **646036-51-3P**
(preparation of diphenylazetidinone peptide derivs. for treating disorders of lipid metabolism)

RN 646036-51-3 HCAPLUS

CN Glycine, N-[[4-[1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-oxo-2-azetidinyl]phenoxy]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D205-08
ICS C07D409-12; A61K031-397; A61P003-06; A61P009-10

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT **646036-51-3P 646036-61-5P 646036-63-7P**
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**646524-22-3P 646524-31-4P**
(preparation of diphenylazetidinone peptide derivs. for treating disorders of lipid metabolism)

IT **646036-52-4P 646036-53-5P 646036-54-6P**
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**646524-14-3P 646524-20-1P 646524-25-6P**
**646524-28-9P**

(preparation of diphenylazetidinone peptide derivs. for treating disorders of lipid metabolism)

IT 439088-73-0P 439088-74-1P 501692-72-4P 501692-73-5P
501692-76-8P 646036-86-4P 646036-87-5P 646036-88-6P
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**646037-03-8P 646037-04-9P 646037-05-0P**
**646037-06-1P 646037-07-2P 646037-08-3P**
**646037-09-4P 646037-10-7P 646037-11-8P**

(preparation of diphenylazetidinone peptide derivs. for treating disorders of lipid metabolism)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L25           1 SEA SSS FUL L23 (      3 REACTIONS)
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